Original article

Comparison of the Disease Activity Score and Juvenile Arthritis Disease Activity Score in the juvenile idiopathic arthritis

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Abstract

Introduction: The assessment of the activity of rheumatoid arthritis and juvenile idiopathic arthritis is made by means of the tools DAS-28 and JADAS, respectively.

Objective: To compare DAS-28 and JADAS with scores of 71, 27 and 10 joint counts in juvenile idiopathic arthritis.

Method: A secondary analysis of a phase III placebo-controlled trial, testing safety and efficacy of abatacept was conducted in 8 patients with 178 assessment visits. Joint count scores for active and limited joints, physician’s and parents’ global assessment by 0–10 cm Visual Analog Scale, and erythrocyte sedimentation rate normalized to 0–10 scale, in all visits. The comparison among the activity indices in different observations was made through Anova or adjusted gamma model. The paired observations between DAS-28 and JADAS 71, 27 and 10, respectively, were analyzed by linear regression.

Results: There were significant differences among individual measures, except for ESR, in the first 4 months of biological treatment, when five of the eight patients reached ACR-Pedi 30, with improvement. The indices of DAS-28, JADAS 71, 27 and 10 also showed significant difference during follow-up. Linear regression adjusted model between DAS-28 and JADAS resulted in mathematical formulas for conversion: [DAS-28 = 0.0709 (JADAS 71) + 1.267] \( R^2 = 0.49 \); [DAS-28 = 0.084 (JADAS 27) + 1.7404] \( R^2 = 0.47 \) and [DAS-28 = 0.1129 (JADAS-10) + 1.5748] \( R^2 = 0.50 \).

Conclusion: The conversion of scores of DAS-28 and JADAS 71, 27 and 10 for this mathematical model would allow equivalent application of both in adolescents with arthritis.
Comparação entre o Disease Activity Score e o Juvenile Arthritis Disease Activity Score na artrite idiopática juvenil

Resumo

Introdução: A avaliação de atividade da artrite reumatoide e da artrite idiopática juvenil é feita por meio de instrumentos distintos, respectivamente pelo DAS-28 e pelo JADAS. Objetivo: Comparar o DAS-28 e o JADAS com a pontuação de 71, 27 e 10 articulações, na artrite idiopática juvenil. Método: Foram avaliadas 178 visitas em oito pacientes com artrite idiopática juvenil, participantes de um ensaio clínico controlado de fase III, testando eficácia e segurança do abatacept. Pontuaram-se as articulações ativas e limitadas, a avaliação global pelo médico e pelos pais em escala analógica visual de 0-10 cm e a velocidade de hemossedimentação convertida em escala de 0-10, em todas as visitas. A comparação entre os índices de atividade entre diferentes observações foi por Anova ou modelo ajustado Gama. As observações pareadas entre o DAS-28 e o JADAS 71, 27 e 10, respectivamente, foram analisadas por meio de regressão linear.

Resultados: Houve diferença significativa entre as medidas individuais, exceto a VHS, nos primeiros quatro meses de tratamento com biológico, quando cinco entre os oito pacientes atingiram a resposta ACR-Pedi 30, com melhoria. Os índices DAS-28, JADAS 71, 27 e 10 também apresentaram diferença relevante durante o período de observação. O ajustamento por meio de regressão linear entre o DAS-28 e o JADAS resultou em fórmulas matemáticas para conversão: [DAS-28 = 0,0709 (JADAS 71) + 1,267] ($R^2 = 0,49$); [DAS-28 = 0,084 (JADAS 27) + 1,7404] ($R^2 = 0,47$) e [DAS-28 = 0,1129 (JADAS 10) + 1,5748] ($R^2 = 0,50$).

Conclusão: A conversão da pontuação do DAS-28 e do JADAS 71, 27 e 10 por esse modelo matemático permitiria a aplicação equivalente de ambos em adolescentes com artrite.

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Assessment Questionnaire (HAQ). Both evaluate the degree of difficulty and independence in activities of daily life in eight domains of functional capacity, also considering the pain and discomfort through aggregated VAS (0–10 cm). Functional capacity is included among the response measures of ACR Pedi 30.

The present study is a secondary analysis of a placebo-controlled, phase III clinical trial, to evaluate the efficacy and safety of intravenous abatacept in patients with active polyarticular JIA and unresponsive to treatment with antirheumatic therapy with methotrexate (MTX). Patients selected for clinical trials have more intense activity and are resistant to conventional treatment, showing more enhanced differences of clinical response. Thus, this sample was considered optimal to compare different continuous measures of activity.

The aim was to explore score equivalence of the tool DAS28 and JADAS with scores of 71, 27 and 10 joints, respectively, in children and adolescents with JIA.

**Subjects and method**

One hundred and seventy-eight visits were assessed of eight patients with JIA who participated in a controlled clinical phase III trial testing the efficacy and safety of abatacept [11,12] and using the same evaluations at intervals of 4 to 12 weeks of the original trial, a withdrawal study design, [11,12] which included an open-label phase of 4 months, double-blind phase trial open-label extension phase of up to 5 years. In the double-blind period, assessments were monthly performed, and in other periods, complete assessments, including measures of activity, were performed every 3 months. The same clinical, laboratory and functional parameters of the clinical trial for the calculation of activity rates of DAS28 and JADAS-71, 27, 10 were used. The protocol of secondary study was approved by the Ethics Committee in Institutional Research (no. 345/2009) of 14 September 2009.

Data were collected from first to last visit with complete joint assessment. Of the eight subjects included, five completed the open phase of induction and the double-blind phase, extension open-label phase. Of the five who concluded the double-blind period, two were given placebo and three were given the study medication. Three subjects concluded the open period, but were not approved for the double-blind since they did not reach ACR-Pedi 30 response, staying in the open-label extension indicated by the protocol. Four subjects left the study in the extension phase in different periods, due to lack of medication efficacy, with change of treatment being necessary. Three subjects concluded the 5 years of extension phase.

Standardized joint assessment (it is more specific for the technical procedure) was performed by the same observer throughout the study. Within the same joint assessment of each valid visit, JADAS-71, 27 and 10 were scored alongside DAS28. To calculate JADAS 71, the score includes 71 joints, with more comprehensive examination including the joints of the lower and upper extremities, spine, and temporomandibular joint. In JADAS-27, the following joints are scored: cervical spine, elbows, wrists, metacarpophalangeal from 1 to 3, proximal interphalangeal, hips, knees and ankles. Regarding JADAS-10, the upper score is 10, that is, if a patient has 15 or 20 active joints, the maximum score to be assigned will be 10.

JADAS final score is calculated by the sum of four components: global assessment of arthritis activity by a physician, measured in a 10-cm VAS, where zero indicates no activity and 10, maximum activity; global assessment by parents/patients also measured on a 10-cm VAS, where zero indicates no activity and 10, the maximum activity perceived by parents or by the patient; active joints count of zero-71 joints and ESR converted to a scale from zero-10 = [VHS mm/h – 20/10] with values over 120 mm/h being converted to 120.

The following joints were assessed for scoring DAS 28: shoulders (2), elbows (2), wrists (2), metacarpophalangeal (10), proximal interphalangeal (10) and knees (2). The joints with pain and edema are independently scored, in addition to the global assessment of activity by the patient, which in this study was performed either by the parents or by the patient him/herself, according to age, being measured on a 10-cm VAS in which zero indicates no disease activity and 10, maximum activity, according to the patient’s perception. In this study, scales scores were performed by the parents regardless of age. DAS28 score was calculated using the following formula in Microsoft Excel:

\[
DAS28 = 0.56 / \sqrt{\text{number of joints with pain}}(28) + 0.28 / \sqrt{\text{number of joints with swelling}} + 0.70 \log (\text{ESR}) + 0.014 \; \text{global VAS}.
\]

Functional capacity, as an integral parameter for the calculation of ACR-Pedi-30 response, was assessed by the CHAQ score with values of zero-3, with 3 meaning the maximum disability scale.

**Statistics analysis**

A descriptive analysis was carried out of baseline variables obtained during patient selection and with calculation of average, standard deviation, median and quartiles for quantitative variables, as well as frequencies and percentages for qualitative variables.

A longitudinal analysis of variables was performed using a repeated measure model through analysis of variance (ANOVA) followed by Tukey’s multiple comparisons test for data showing symmetrical distribution. The adjustment of a generalized linear model for repeated measures, with Gamma distribution, was performed for the data that showed an asymmetric distribution.

For comparative evaluation between DAS28 and JADAS in three versions (71, 27 and 10), a linear regression was performed by applying the ANOVA test for data with normal distribution. As for the comparison between JADAS-71, JADAS-27 and JADAS-10, a model with Gamma distribution was adjusted.

All analyses were performed using SAS for Windows, v.9.2. In all tests, we used a significance level of 5% or the corresponding p-value.
Table 1 – Clinical, anthropometric, laboratorial, activity and functional parameters in eight patients during the first evaluation of selection for the clinical trial.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Average</th>
<th>Standard deviation</th>
<th>Median</th>
<th>Q1</th>
<th>Q3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>137.6</td>
<td>39.5</td>
<td>136.2</td>
<td>110.8</td>
<td>162.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>31.9</td>
<td>11.4</td>
<td>32.4</td>
<td>23.4</td>
<td>39.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>135.5</td>
<td>18.6</td>
<td>139.7</td>
<td>124</td>
<td>149.5</td>
</tr>
<tr>
<td>No. of active joints</td>
<td>24</td>
<td>10.5</td>
<td>20.5</td>
<td>18</td>
<td>30.5</td>
</tr>
<tr>
<td>No. of limited joints</td>
<td>20.3</td>
<td>11.6</td>
<td>16.5</td>
<td>15</td>
<td>26</td>
</tr>
<tr>
<td>No. of joints with edema</td>
<td>19.6</td>
<td>10</td>
<td>20</td>
<td>12.5</td>
<td>28</td>
</tr>
<tr>
<td>No. of joints with pain</td>
<td>12</td>
<td>13.3</td>
<td>8.5</td>
<td>4.5</td>
<td>11.5</td>
</tr>
<tr>
<td>Physician’s VAS (0–10 cm)</td>
<td>5.5</td>
<td>1.3</td>
<td>5.8</td>
<td>5.3</td>
<td>6.3</td>
</tr>
<tr>
<td>Parents’ VAS (0–10 cm)</td>
<td>3.6</td>
<td>2.2</td>
<td>3.1</td>
<td>1.8</td>
<td>5.6</td>
</tr>
<tr>
<td>Pain VAS (0–10 cm)</td>
<td>3.2</td>
<td>2.1</td>
<td>2.4</td>
<td>2.2</td>
<td>5.3</td>
</tr>
<tr>
<td>CHAQ DI (0–3)</td>
<td>1.2</td>
<td>0.5</td>
<td>1.2</td>
<td>0.8</td>
<td>1.8</td>
</tr>
<tr>
<td>JADAS-71 (0–101)</td>
<td>10.1</td>
<td>12</td>
<td>6.1</td>
<td>4</td>
<td>14.1</td>
</tr>
<tr>
<td>JADAS-27 (0–57)</td>
<td>8.7</td>
<td>10</td>
<td>5.7</td>
<td>0.4</td>
<td>11.5</td>
</tr>
<tr>
<td>JADAS-10 (0–40)</td>
<td>7.9</td>
<td>7.6</td>
<td>6.1</td>
<td>3.9</td>
<td>13</td>
</tr>
<tr>
<td>DAS-28 (0–7.8)</td>
<td>4.8</td>
<td>1</td>
<td>4.8</td>
<td>3.9</td>
<td>5.2</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>36.2</td>
<td>10.3</td>
<td>35</td>
<td>30</td>
<td>45</td>
</tr>
</tbody>
</table>

Q1, first quartile; Q3, third quartile; VAS, visual analogical scale; CHAQ-DI, Childhood Health Assessment Questionnaire Disability Index; JADAS, Juvenile Arthritis Disease Activity Score; DAS-28, Disease Activity Score; ESR, erythrocyte sedimentation rate.

Results

Three boys and five girls were assessed, all diagnosed with JIA and aged 7–17 years, with a case classified as systemic and seven as polyarticular, with two being positive for rheumatoid factor (latex test). Clinical, anthropometric, laboratory and activity variables of arthritis, including the functional indices in the first evaluation, are presented in Table 1.

With the use of ANOVA a significant difference was found in the visits which took place for selection and those after 4 months of treatment for all indices, when five patients met the criteria of ACR Pedi 30 response, that is, there was improvement in 30% of at least three of the six key variables.

Longitudinal comparison showed that there was asymmetric distribution of CHAQ, DAS28, JADAS-71, 27 and 10 variables, and the adjustment of the model with Gamma distribution showed statistically significant difference within the assessments (p < 0.05), with the highest rates being in the first and in the second evaluation, respectively, at the selection and after 4 months of biological treatment in open phase. The other visits included a total of 30 serial evaluations, monthly, within 6 months of the double-blind phase, and quarterly in the evaluations that followed during the open-label extension. These evaluations were compared, but no significant difference was found in all the individual parameters for the calculation of the indices and items of DAS28 and JADAS-71, 27 and 10. No significant difference was observed within the respective versions of JADAS-71, 27 and 10. For this comparison, we also adjusted a model with Gamma (p = 0.5) distribution.

The linear regression analysis of JADAS-71, 27 and 10 and DAS 28 resulted in conversion formulas among the scales, the regression analysis of which is shown in Fig. 1:

\[ \text{DAS} 28 = 0.0709 \times \text{JADAS-71} + 1.267 \quad (R^2 = 0.49). \]

\[ \text{DAS} 28 = 0.084 \times \text{JADAS-27} + 1.7404 \quad (R^2 = 0.47). \]

\[ \text{DAS} 28 = 0.1129 \times \text{JADAS-10} + 1.5748 \quad (R^2 = 0.50). \]

Discussion

The presented results support the equivalence between the DAS-28 and JADAS in three versions, with joint counts of 71, 27 or 10, respectively, through longitudinal observation made during a controlled clinical trial in polyarticular JIA. Besides DAS28, there are other instruments used for RA, such as the Clinical Disease Activity Index (CDAI), among others, but of limited use in pediatric patients.

Continuous measures such as DAS28 and JADAS have the advantage of establishing absolute values, identifying changes in clinical status by a number on a continuous scale. The straightforward calculation makes the method feasible in daily practice, just as in clinical trials. However, there are few publications reporting the use of DAS28 in JIA.

Measures in absolute values provide better consistency of assessment among physicians and allow patients to understand the significance of their disease activity via an absolute number. The corresponding measures for JIA were recently developed and three versions of the tool JADAS allowed to equate the different presentations of JIA according to the ILAR classification.

One must also consider that the joint counts of the DAS28 omit the lower limb joints, but in the JIA the involvement of the lower extremities is predominant. Measures of perceived activity of arthritis by the physician, the patient him/herself or their parents, as well as ESR or CRP, implement the composite measures, weighing up several competing factors for the activity status.

In JADAS validation study, as well as in a recent study, which used CRP to replace ESR, results of JADAS-71, 27 and 10 kept the correlation among them and with the other activity parameters. Also, McErlane et al. recently calculated JADAS with only three variables, excluding ESR for broader applicability, and reported a correlation of measures and their metric equivalence.

One must consider, however, that in this study VAS scores by the patient him/herself as conceived in DAS28 was replaced
by the score of the scale performed by the parents. It is also known that, regardless of age, caregiver’s perception may substantially differ from the perception of the patient at any age.

Among the other limitations of this analysis we find the small sample that limits the power of the study, and the selection of children enrolled in clinical trials. If, on one hand, the population sample would provide greater variability of activity, strict control of all measures and standardized joint examination, by the same observer at regular intervals, in addition to the parallel evaluation of response measures (ACR-Pedi-30) to establish responders, the response pattern in the period of greatest activity when selecting for testing, were the favorable points to test this equivalence.\(^\text{17}\)

There is practical applicability of the results to patients with JIA, because, besides the simple and direct score, the individual measures of clinical parameters can be conducted in daily practice. The use of metric conversion may also be useful in specific situations of transition from adolescent to adult condition. As an example, a patient diagnosed with JIA at 15 years and another diagnosed with RA at 17 could be evaluated by calculating the equivalence of the instruments used.

**Conflicts of interest**

The authors declare no conflicts of interest.

**REFERENCES**

